

Figure 1 : Alignment of N-terminal fragments of Human Hedgehog Proteins

1  
Indian CGPGRVVGSR RRPPRK-LVP LAYKQFSPNV PEKTLGASGR YEGKIARSSE  
Sonic CGPGRGFG-K RRHPKK-LTP LAYKQFIPNV AEKTLGASGR YEGKISRNSE  
Desert CGPGRGPVGR RRYARKQLVP LLYKQFVPGV PERTLGASGP AEGRVARGSE

51  
Indian RFKELTPNYN PDIIFKDEEN TGADRLMTQR CKDRLNSLAI SVMNQWPGVK  
Sonic RFKELTPNYN PDIIFKDEEN TGADRLMTQR CKDKLNLAI SVMNQWPGVK  
Desert RFRDLVPNYN PDIIFKDEEN SGADRLMTER CKERVNALAI AVMNMWPGVR

101  
Indian LRVTEGWDED GHHSEESLHY EGRAVDITTS DRDRNKYGLL ARLAVEAGFD  
Sonic LRVTEGWDED GHHSEESLHY EGRAVDITTS DRDRSKYGML ARLAVEAGFD  
Desert LRVTEGWDED GHHAQDSLHY EGRALDITTS DRDRNKYGLL ARLAVEAGFD

151  
Indian WVYYESKAHV HCSVKSEHSA AAKTGG SEQ ID NO: 23  
Sonic WVYYESKAHI HCSVKAENSV AAKSGG SEQ ID NO. 24  
Desert WVYYESRNV HVSVKADNSL AVRAGG SEQ ID NO. 25

Gap(s), indicated by -, added to facilitate alignment

09883848.06.180.1

Figure 2: SEQ ID NO: 26 is the consensus sequence of a hedgehog protein suitable for use in developing the conjugated proteins of the invention, antagonist, where "Xaa" indicates amino acids that differ between the Sonic, Indian and Desert hedgehog proteins.

C\* G P G R Xaa1 Xaa2 Xaa3 Xaa4 Xaa5 R R Xaa6 Xaa7 Xaa8 K Xaa9 L Xaa10 P  
L Xaa11 Y K Q F Xaa12 P Xaa13 V Xaa14 E K T L G A S G R  
Xaa15 E G K Xaa16 Xaa17 R Xaa18 S E R F K Xaa19 L Xaa20 P N Y N  
P D I I F K D E E N Xaa21 G A D R L M T Xaa22 R  
C K Xaa23 Xaa24 Xaa25 N S L A I Xaa26 V M N Xaa27 W P G V K  
L R V T E G W D E D G H H Xaa28 Xaa29 Xaa30 S L H Y  
E G R A V D I T T S D R D R Xaa31 K Y G Xaa32 L  
A R L A V E A G F D W V Y Y E S Xaa33 Xaa34 H Xaa35  
H Xaa36 S V K Xaa37 Xaa38 Xaa39 S Xaa40 A A Xaa41 Xaa42 G G

Where

C\* is a cysteine that may be modified, altered or substituted within another moiety or series of moieties as described herein;

|                            |                            |                             |
|----------------------------|----------------------------|-----------------------------|
| Xaa1 is either V or G;     | Xaa2 is either V, E or P   | Xaa3 is either G or V       |
| Xaa4 is either S or G;     | Xaa5 is either R or K;     | Xaa6 is either P, H or Y;   |
| Xaa7 is either P or A;     | Xaa8 is either R or K;     | Xaa9 is any amino acid;     |
| Xaa10 is either V or T;    | Xaa11 is either A or L;    |                             |
| Xaa12 is either S, I or V; | Xaa13 is either N or G;    | Xaa14 is either P or A;     |
| Xaa15 is either Y or A;    | Xaa16 is either I or V;    | Xaa17 is either A or S;     |
| Xaa18 is either S, N or G; | Xaa19 is either E or D;    | Xaa20 is either T or V;     |
| Xaa21 is either T or S;    | Xaa22 is either Q or E;    | Xaa23 is either D or E;     |
| Xaa24 is either R or K;    | Xaa25 is either L or V;    | Xaa26 is either S or A;     |
| Xaa27 is either Q or M;    | Xaa28 is either S or A;    | Xaa29 is either E or Q;     |
| Xaa30 is either E or D;    | Xaa31 is either N or S;    | Xaa32 is either L or M;     |
| Xaa33 is either K or R;    | Xaa34 is either A or N;    | Xaa35 is either V or I;     |
| Xaa36 is either C or V;    | Xaa37 is either S or A;    | Xaa38 is either E or D;     |
| Xaa39 is either H or N;    | Xaa40 is either A, V or L; | Xaa41 is either K or R; and |
| Xaa42 is either T, S or A. |                            |                             |